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EXAMINER	
CAPUTA, A	
ART UNIT	PAPER NUMBER
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DATE MAILED: 06/14/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3/10/95 3/13/95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-12, 17, 19-21 are pending in the application.
   Of the above, claims 2, 3, 6, 9-11 are withdrawn from consideration.
2. ☒ Claims 13-16, 18 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1, 4, 5, 7, 8, 12, 17, 19-21 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Part III DETAILED ACTION

1. Applicants' amendment (Paper No. 18) was received. Claims 13-16, and 18 are cancelled. Claims 1-12, 17, 19-21 are pending. Claims 2, 3, 6, and 9-11 are withdrawn from consideration. Claims 1, 4, 5, 7, 8, 12, 17, 19-21 are being examined only to the extent that the claimed invention reads on the nucleic acid sequence comprising PB2 (SEQ ID Nos. 15 and 29), the species elected by applicants.

2. The text of those sections of Title 35 U.S.C. not included in this action can be found in a prior Office Action.

3. The information disclosure statement received fails to comply with the provisions of MPEP 609 because copies of the abstract of Herlocher et al., abstract of Castrucci, article of Kilbourne, and article by WHO were **not** provided.

Until a substitute IDS along with the requested references is provided as indicated by applicants said references have not be considered to the merits as set forth in the last Office Action.

4. The prior objection to the use of trademarks is withdrawn in view of applicants' amendment.

5. The prior objection to the disclosure is maintained. Applicants state that a preliminary amendment was filed 7/22/93 with the insertion of the accession numbers of the wild type and cold adapted strain.

Applicants' amendment is not of record. Accordingly, said objection is maintained as set forth in the last Office Action.

6. The prior rejection of claims 1, 4, 5, 7-8, 12, and 17 under

35 U.S.C.§ 112, 2nd paragraph is withdrawn in view of applicants' amendment and arguments.

7. The prior objection to the specification under 35 U.S.C. § 112, first paragraph, as failing to adequately teach one of ordinary skill in the art how to make and/or use the claimed invention, i.e. failing to provide an enabling disclosure is maintained.

The elected species is drawn to reassortant virus containing said nucleic acid which has at least one surface antigen of the wild type and the PB2 of the cold adapted virus. However, the specification provides insufficient guidance to using the elected species reassortant as a vaccine. As exemplified by the prior art it appears more than the PB2 is required since other genes such as PA, M. PB1 contribute to attenuation (see Snyder et al., particularly abstract).

Applicants essentially argue that the ferret model as disclosed in the specification (see page 13) is an accepted model. It is the Examiner's position that it is unpredictable using the ferret model to establish attenuation since Snyder et al. teach the ferret is not sufficient to predict the outcome of attenuation of the vaccine since ferrets have a normal body temperature higher than humans (see page 491). Accordingly, in view of the teachings of Snyder et al. it is unpredictable if the attenuation of the wt(2), cold adapted virus, reassortant, or the gene encoding the PB2 (wild type or cold adapted) as described in the specification is sufficiently attenuated for use in humans.

Applicants assert the Examiner has failed to indicate to applicants how they have failed to teach one skilled in the art how to use the claimed invention. Applicants arguments are not persuasive. Since claimed invention recites the use of the reassortant as a vaccine and the art discloses the ferret is not

useful to predict the outcome of attenuation of the vaccine it the Examiner's position it is unpredictable and be an undue burden for a skilled artisan in the art to determine if the claimed invention would have been useful as a vaccine.

Applicants have not shown how the claimed composition is useful as a vaccine despite the summary of Examples 1-10. The Examples as set forth above do not show any further evidence how to use the claimed composition as a vaccine. Said Examples at best only provide procedures for conducting clinical studies (see Example 10), clinical studies of influenza virus vaccines which are not commensurate in scope with the claimed invention (see Example 6), and use of the viruses of the present invention as vectors for foreign proteins (see Example 9). For the reasons set forth above and in the last Office Action said rejection is maintained.

The Examiner withdraws the objection to a reassortant containing genes from influenza A and B upon further consideration.

8. The prior rejection of claims 12, 13, 17 and newly amended claims 12, 17, 19, and 20 under 35 U.S.C. § 112, first paragraph, is maintained for the reasons set forth in the last Office Action.

9. The prior rejection of claims 1-4, 5, 7-8 under 35 U.S.C. § 112, first paragraph, is withdrawn in view of applicants' amendment and arguments.

10. The prior rejection of Claims 1 and 4 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Buonagurio et al. (J. Virol.

49(2):418-425 1984) is withdrawn in view of applicants' amendment.

11. The prior rejection of claims 1, 4, 5, 7, 8, 12, 13, 14, 17, and 18 and newly amended claims 1, 4, 5, 7, 8, 12, 17, and 19-21 under 35 U.S.C. § 103 as being unpatentable over Cox et al. (Virology 167:554-567 1988) and further in view of Belshe et al. (J. Infectious Disease 149(5): 735-740 May 1984 or Belshe et al. (J. Infectious Disease 165: 727-732 April 1992) is maintained.

Cox et al. teach the entire nucleotide sequence (i.e. DNA sequence) for the PB2 gene of the wt and ca A/Ann Arbor/6/60 virus (see Figure 6, page 561, and Table 1). Cox et al. teach reassortant viruses that received the HA and NA from the wild type virus and the other genes of the ca parent are sufficiently attenuated, immunogenic and protective in humans (see page 554 and 565). Accordingly, it would have been obvious to one of ordinary skill in the art for one of ordinary skill that a vaccine for administration for humans encompass PB2 of the cold adapted donor since said gene contributes to the attenuation of reassorted virus. It is noted the claimed invention is directed to a PB2 sequence of a wild type virus and (cold adapted virus derived thereof) which was passaged through the egg twice and the PB2 sequence of the wild type virus as disclosed in the prior art was passaged in egg several times. While it is true that there may be difference in the nucleic acid sequence of the nucleic acid sequence of the PB2 of the prior art and as claimed it is reasonable to expect the that there are an obvious or analogous variant of each other since they appear to have the same functional properties (i.e. both appear to be useful as for the development of a vaccine comprising a reassortant which uses the cold adapted mutant as the donor strain and the HA and NA

(surface antigens) are from an epidemic variant virus (wild type)).

Cox et al. does not teach of a method of preventing influenza in patients using the reassortants nor of using reassortant containing a wild type HA and NA from such wild type influenza viruses as California/10/78 (H1N1) virus, A/Kawasaki/9/86 (H1N1) virus, A/Korea/1/82, and B Texas/1/84.

Belshe et al. (J. Infectious Disease 149(5): 735-740 May 1984) teach a method of preventing influenza comprising a reassortant containing six genes of the cold adapted influenza A/AnnArbor/6/60 virus and the HA and NA of the wild type California/10/78 (H1N1) virus.

Belshe et al. (J. Infectious Disease 165: 727-732 April 1992). teach a method of preventing influenza comprising a reassortant containing six genes of the cold adapted influenza A/AnnArbor/6/60 virus or B/AnnArbor/1/66 and the HA and NA of the wild type A/Kawasaki/9/86 (H1N1) virus, A/Korea/1/82, B Texas/1/84. It would have been obvious to one of ordinary skill in the art to use the method of immunization as described by Belshe et al. for reassortant as taught by Cox et al. or Belshe et al. since Belshe et al. teaches a method of immunization which is effective for a reassortant containing the cold adapted influenza A/AnnArbor/6/60 parent virus. It would have been obvious to one of ordinary skill in the art to optimize the dosage of the vaccine for maximal efficacy.

Applicants argue that Cox et al. does not suggest applicants PB2 segment, because the sequence as set forth by Cox et al. is different from applicants. While it is true that there may be difference in the nucleic acid sequence of the PB2 of the prior art and as claimed it is reasonable for one of ordinary skill in the art to expect the that there are an obvious or analogous variant of each other since they appear to have the

same functional properties (i.e. both useful for the development of a vaccine, both are comprised of a reassortant which uses the cold adapted mutant as the donor strain and the HA and NA (surface antigens) from an epidemic variant virus). Accordingly, for the reasons set forth above and in the last Office Action said rejection is maintained.

New Grounds of Rejection

12. Claims 1, 4, 5, 7, 8, 12, 17, 19-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 5, 7, 8, 12, 17, 19-21 are rejected for being vague and indefinite for use of the transition phrase " consisting essentially" to further limit a compound (i.e nucleic acid) since said phrase is used to limit a composition and not a compound.

13. Applicants' amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The

examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ms. Christine Nucker, can be reached on (703)-308-4028

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-308-4227.

Anthony C. Caputa, Ph.D.
June 12, 1995

Primary MARY E. MOSHER
PATENT EXAMINER
GROUP 1800